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COMPANY SANITIZED

May 4, 1994

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Document Processing Center (7407)  
(Attn.: Section 8(e) Coordinator)  
Office of Pollution Prevention and Toxics  
U. S. Environmental Protection Agency  
401 M Street, SW  
Washington, DC 20460

8EHQ-94-13017  
88940000 259

RE.: 8EHQ-0991-1348 and 8EHQ-1091-1357; TSCA Section 8(e) Notice; R&D Pesticidal  
Chemical, CGA-248757, Supplemental Submission

Dear Section 8(e) Coordinator:

Ciba-Geigy Corporation (Ciba) requests that the specific chemical identity and CAS Registry Number shown in brackets in this letter be treated as Confidential Business Information. We enclose a sanitized copy of this letter for the public file.

Ciba previously submitted four additional 8(e) notices for CGA-248757 as indicated below.

- a) September 18, 1991: Preliminary results from two positive *in vitro* genotoxicity studies (8EHQ-0991-1348).
- b) September 27, 1991: Four-week feeding study in mice; Four-week feeding study in rats; Four-week feeding study in ICR mice; Four-week feeding study in mice (liver, kidney, spleen, thymus, and bone marrow effects). (Assigned new document control number 8EHQ-1091-1357).
- c) November 30, 1993: Preliminary information (chromosome aberrations) from a cytogenic test on human lymphocytes.
- d) March 10, 1994: Preliminary information from a recently completed mouse oncogenicity study in mice (treatment related increase in liver masses).

In accordance with the EPA's March 16, 1978, policy statement on Section 8(e) reporting under the Toxic Substances Control Act and EPA's June 1991 TSCA Section 8(e) Reporting Guide, Ciba wishes to bring to your attention certain preliminary information from a chronic toxicity/oncogenicity study in rats and from a multigeneration reproduction study in rats conducted in the laboratories of Ciba Plant Protection Environmental Health Center in

Farmington, Connecticut, with the R&D compound, [ ], CAS Registry No. [ ]. The substance, also known as CGA-248757, may be referred to in the public file as a "substituted bicyclic dione."

1. Chronic Toxicity/Oncogenicity Study in Rats:

CGA 248757 technical was administered in the diet to groups of 60 or 70 (control and high dose) rats at concentrations of 0, 5, 50, 3000 ppm (both sexes), 5000 ppm (males only), or 7000 ppm (females only) for two years. The incidences of masses observed at necropsy in the pancreas of the male rats were 1/70, 2/60, 2/60, 8/60, and 15/70 at 0, 5, 50, 3000, and 5000 ppm, respectively. The incidence of pancreatic masses in treated females was not increased in a statistical or dose-related manner. Grossly observed pancreatic masses can represent lymph nodes as well as divergent types of lesions ranging from enlarged blood vessels and inflammatory foci to assorted neoplasms (i.e., islet cell, exocrine cell, multicentric, and secondary types). The incidences of this gross necropsy observation, however, are suggestive of a treatment-related effect. These preliminary necropsy observations have not been through quality assurance review or subjected to/confirmed by histopathologic evaluation.

2. Multigeneration Reproduction Study in Rats:

CGA 248757 technical was administered in the diet to groups of 28 male and 28 female rats at concentrations of 0, 25, 500, or 5000 ppm through two successive generations. Mean pup body weights were significantly reduced at 5000 ppm on lactational days 0, 7, 14, and 21 in the first generation and on lactational days 0, 14, and 21 in the second generation. No other reproductive/developmental parameters were affected. In addition, treatment-related histopathologic liver lesions were observed in males at 500 ppm and both males and females at 5000 ppm, including hepatocellular vacuolation and nuclear swelling, and an accumulation of granular, yellow-green to golden-brown pigment in enlarged Kupffer cells. There was also an apparent increase in the incidence/severity of biliary hyperplasia in all animals at 5000 ppm.

CGA 248757 is a research and development compound being evaluated for pesticidal purposes. These evaluations are being conducted in the United States under the supervision of technically qualified personnel, knowledgeable in handling potentially hazardous chemicals.

In response to these new findings, Ciba will do the following:

1. Revise the Material Safety Data Sheet to reflect these findings.
2. Notify persons working with this compound of the new findings in accordance with the notification requirements of OSHA's Hazard communication Standard (29 CFR 1910.1200).
3. Provide EPA with copies of the final study reports after we receive them.

Please contact the undersigned if you need any additional information.

Very truly yours,



Anthony Di Battista

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